Clinical Aspects of the Encephalitides*

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ENCEPHALITIS is an non-specific term, both anatomically and etiologically. Anatomically, few patients show involvement of the encephalon alone; in addition to variable degrees of damage here, there will also be some amount of meningitis, myelitis, or neuritis, singly or in combination. Etiologically, there are several viruses now known which cause primary encephalitis. There are also a few cases which follow certain immunization procedures, and a relatively large number secondary to other infections which are usually but not always of virus origin. These secondary cases may be and probably are due to the original infecting agent, though there is some support for the idea that they are caused by some other unknown agent or by toxins elaborated by the original agent or by some allergy-like reaction to it.

With so many variables and unknowns, it is obvious that there can be no such thing as *the* clinical picture of encephalitis. Final, undebatable diagnosis often must rest on virus neutralization and complement fixation studies. Routine blood counts may vary widely, though there is likely to be an increase in white cells with a predominance of polymorphonuclears. Spinal fluid findings also vary, with nothing characteristic of any given type of the disease. Sometimes the fluid is entirely normal; nearly always there is a moderate increase in pressure and in proteins, and an increase in cells which are usually lymphocytes. Thus this paper must be confined to the general clinical pattern of the various encephalitides, and may be most inaccurate in any single case.

ENCEPHALITIS A

The first and historically the most important type of primary encephalitis is the one described by von Economo and often called by his name. This disease has also been called lethargic encephalitis (which in many cases is a misnomer), epidemic encephalitis, and more recently encephalitis A. It is rarely seen at present, but it has occurred in widespread epidemics in this country and elsewhere.

This disease usually occurs during the winter season. Its incubation period is not known; it is thought to be about ten days in most cases, but it may vary from a few days to several weeks. It may involve any age, but is most common between 10 and 30 years. The mode of spread is not known, but direct transmission is rare.

In the classical case there are three stages: the acute stage, lasting from a few days to several months; a stage of remission, during which the patient may be well or nearly so, lasting up to several years; and a chronic stage which gradually appears and may well last until death. Not infrequently the first stage does not occur or is not recognized, in which case the first known evidence of the disease is the appearance of the chronic symptoms.

The first stage may be most variable. Five types are described; these, with their intergradations, make possible an infinite variety of detail. These types in brief are: (1) the somnolent, with little fever, and usually with marked extraocular palsies which are variable and changing; (2) the excited and overactive, with high fever, delirium, spinal root pain, involuntary movements, and pupillary changes, but with little paralysis; (3) the early Parkinson, with immobility, slow weak movements, insomnia and sleep reversal; (4) the fulminant, with high fever, delirium, convulsions, and often early death; and (5) the abortive, with transient pains, diplopia, headache, insomnia, and myoclonic movements. Neither the type nor the severity of stage I bears any constant relationship to the events to come in stage III.

The remission following the acute stage may not be one of complete normality. There may be pupillary or oculomotor defects, rigidity, ataxia, behavior or personality changes, or mental defects.

The symptoms of the chronic stage advance slowly and uniformly, without fever or acute signs. They include Parkinsonism; choreiform movements; tics and tremors; dystonia; cranial, bulbar, and spinal paralyses; convulsions; mental and personality changes; anesthesia and hyperesthesia; sleep disturbances; and a wide variety of autonomic and metabolic changes.

Mortality in the acute stage has ranged from as little as 10 per cent in some epidemics to as high as 70 per cent in others. The prognosis for complete and permanent recovery is poor.

ENCEPHALITIS B

Encephalitis B includes St. Louis and Japanese encephalitis and Australian X disease so far as clinical and pathologic findings are concerned, though their viruses are not identical and the mortality varies. These infections tend to occur in the summer, and may involve any age though the elderly are more susceptible. The mode of spread is still not known, but it is only rarely by direct contact.

There may be three or four days of systemic prodromes, or the encephalitic symptoms may begin at once, or there may be no nervous signs and a doubtful diagnosis made on spinal fluid changes plus accessory circumstances. The characteristic symptoms are fever, headache, signs of intense meningeal irritation (a cardinal symptom), frequently convulsions, drowsiness or coma, and delirium. The fever is constant, and lasts from three

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or four days to two weeks or more. Psychic disturbances are usual, including hallucinations, depression, confusion, and catalepsy; these last for one to two weeks. Muscular rigidity is very common, as are also involuntary movements of clonic or twitching type. Mild and transient paralyses are also common, involving the bulb with fair frequency. Pupillary changes also occur. The autonomic system is rarely involved.

The mortality of the St. Louis type is about 20 per cent, of the Japanese 33 per cent to 70 per cent, and of Australian X disease 70 per cent. Survivors usually become normal.

EQUINE ENCEPHALITIS

Equine encephalitis is divided into eastern and western types, which are clinically indistinguishable although the eastern tends to be more severe. It is a disease of warm weather, and is more likely to attack persons under ten years of age. It involves horses and mules, and is apparently transmitted from them to man by mosquitoes. There is reason to believe that the basic reservoir of infection may be in domestic or wild birds.

The prodromes begin with fever, headache, and drowsiness which deepens into stupor and coma. Vomiting and convulsions are usual, together with signs of severe meningeal irritation. These symptoms usually last about two weeks.

The mortality is high, in some series as much as 74 per cent; the average for the western strain is 5 to 15 per cent and for the eastern about 65 per cent. Survivors may be normal, but residuals are not rare. These consist of mental defect, personality changes, speech defect, pareses, ataxia, and spasticity.

POST-PASTEUR ENCEPHALITIS

The incidence of post-Pasteur encephalitis is reported as high as 12 per 1000, though general opinion is that the figure should be lower than this. The more completely inactivated virus gives a lower incidence of encephalitis. The symptoms are likely to begin after 10 to 14 days of treatment, and often there is warning in the form of malaise, headache or vomiting, and local reaction at the site of recent injections. The symptoms may be those of disseminated encephalomyelitis, Landry's ascending paralysis, transverse myelitis of the thoracic or lumbar cord, or peripheral neuritis especially of the facial nerves. Mortality is about 15 per cent, with survivors tending to make a good ultimate recovery.

POST-VACCINATION ENCEPHALITIS

Encephalitis following small pox vaccination has been reported as often as once per 1000 vaccinations; on the other hand, millions of vaccinations have been done without a case being noted. It is more common in older people than in infants, and more common in primary than in repeated vaccinations. It usually appears 10 or 11 days after vaccination, with extremes of two to twenty-five days, with headache, fever, vomiting, and convulsions. There is often severe cord injury with flaccid paralysis and sometimes anesthesia. Cranial nerves are rarely involved. The mortality is 30 per cent to 50 per cent, with survivors tending to regain normality.

MUMPS ENCEPHALITIS

There is probably some involvement of the central nervous system in most cases of mumps, if one accepts the evidence of changes in the spinal fluid without symptoms. Clinical findings are said to occur in from 1 per cent to 25 per cent of cases; the disease is usually mild and short, and the number of cases found undoubtedly varies with the alertness of the observer. It tends to occur at about the height of the mumps infection, but it may be found a few days before or after the primary infection or even when no mumps infection is noted. Most commonly the symptoms are limited to those of meningeal irritation, but there may be findings of encephalitis, myelitis, polyneuritis, and deafness. The prognosis is very good both for life and for normality, the only sequel being an occasional deafness.

MEASLES ENCEPHALITIS

Measles encephalitis is undoubtedly the most common of the more severe forms following acute infections, and therefore it will be discussed in some detail as it may serve as a general pattern for the disease as it occurs after influenza, chicken pox, rubella, and other infections.

Its seasonal and age incidence parallels that of measles. Its frequency is probably between one and four cases per 1000 cases of measles; these figures vary in different epidemics, and are inaccurate, as many cases of measles and some of the milder cases of encephalitis are not reported.

The onset of encephalitis may precede the rash of measles, or even precede the first symptom of that disease; or it may be delayed until well into convalescence. Most cases, however, begin in the period between the height of the rash and its disappearance. Symptoms of onset vary greatly. Fever is usually but not invariably present; its duration bears no consistent relationship to other findings. Changes in the sensorium almost always occur, usually as torpor or lethargy which often deepens into coma; but occasionally there may be excitement, restlessness, and disorientation. Convulsive seizures of all types are common, especially in the early stages and sometimes as terminal events.

Cranial nerve irritations and paralyses occur in all varieties; peripheral nerves show tremors, ataxia, paralysis, and paresis; urinary malfunction appears as incontinence, involuntary urination, and retention; and sensory nerves show disorders in pain, anesthesia, hyperesthesia, hypesthesia, and paresthesia. These and other findings occur singly and in combination; they may regress, recur, remain, or disappear.

The most consistent neurological signs are those of meningeal irritation, with one sign or more present in most instances, though a considerable

number is unaffected. Both superficial and deep reflexes are almost certain to show some alteration, though an occasional normal is found. These changes may be either hyper- or hypo-activity, with some tendency to inequality, and all subject to change on later examination.

Laboratory findings share the inconsistency and variability already noted. The white blood cells are usually increased to an average of 16,000 with occasional counts as high as 40,000, with a high percentage of polymorphonuclears; but cases have been reported with counts as low as 2800. Spinal fluid may be normal, and under normal pressure; but this is unusual. In most instances the pressure is moderately elevated, and the fluid contains 50 to 400 cells which are mostly lymphocytes; though occasionally they are polymorphs, especially early in the disease. Protein is usually increased, though here again there is the inevitable exception.

The prognosis for life is uncertain in any individual case, as the disease may progress, regress, or remain stationary. Mortality is about 10 to 20 per cent. About half of the survivors show sequelae of greater or lesser severity. Common and serious among these are personality and behavior changes and mental deterioration, sometimes to the point of idiocy. There may also be ataxia, spasticity, pareses and paralyses, aphasias, sensory disorders, bladder malfunction, sexual precocity, obesity, cachexia, and diabetes mellitus.

There is no specific treatment for this or any other form of encephalitis. In the encephalitis of measles, shock therapy has sometimes been followed by dramatic improvement. This treatment has not been thoroughly established, but I know of no other at present which offers as much encouragement.

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QUESTIONS AND ANSWERS

MODERATOR REIMANN: Dr. Hamilton, in what percentage of cases of measles do the encephalitic symptoms occur?

DR. HAMILTON: There is no way to determine that with certainty, because certainly a great many cases of measles are not reported, and likewise probably a good many milder instances of encephalitis don't get into the figures. It is estimated to run between one and four cases of encephalitis to a thousand cases of measles.

MODERATOR REIMANN: Dr. Hamilton, do you mean by "shock therapy" with typhoid vaccine, the fever produced by the vaccine?

DR. HAMILTON: I have no way of answering whether it is fever or whether it is something else that occurs along with the injection of the foreign proteidin. If you want my guess, I would say that it is probably the latter, for the reason that in a good many instances the temperature, as such, is already very high, without any apparent relief of the symptoms, whereas after the temperature has fallen, a similar fever induced by injection does sometimes improve the clinical aspects.